LETTERS

Diabetic Ketoacidosis in Children

The case report on ketoalkalosis in Rett syndrome by Cameron *et al*., contains some interesting biochemistry.[1] The pO_2 on admission was said to be 36.5 kilopascals. Room air at STP has a partial pressure of oxygen around 20 kilopascals, so I presume this patient was breathing oxygen. If so, how much and why?

The serum osmolality was measured at 334, while calculation suggests that it should have been at least 360. What caused that discrepancy?

I am puzzled also as to why half strength saline was used for rehydration. This patient was not seriously hyperosmolar and half strength saline has been associated with the development of cerebral oedema.

Finally, why should an X-linked disorder affect only females?

P. Daggett
Staffordshire General Hospital, Stafford, UK

Reference

1 Cameron FJ, Hawkins KC, Khadilkar VV, Tasker RC, Preece MA. Insulin-dependent diabetes mellitus presenting with ketoalkalosis in Rett syndrome. *Diabetic Med* 1997; **14**: 884–885.

Diabetic Ketoacidosis in Children: Authors' Reply

We are glad of the opportunity to reply to Dr Daggett's comments. The first blood gas with high PaO_2 was taken shortly after admission to the ward, at a time when the child would have been breathing supplemental oxygen following transportation. A large osmolar gap may occur in certain cases of poisoning, administration of mannitol, and inherited metabolic disorders. We have made an error in using the blood sugar value of 46.1 mmol l^{-1} (it should have been 18.6 mmol l^{-1}). At the time of initial laboratory osmolar measurement of 334 mosmol kg^{-1} the calculated osmolality was 318 mosmol kg^{-1}, which is an abnormally raised osmolar gap (see below). An X-linked disorder can affect only females if it is associated with embryolethality in males which is thought to be true of Rett syndrome.

The issue of fluid administration and the development of cerebral oedema in children with diabetic ketoacidosis remains controversial. Articles and editorials have remarked that efforts to relate fatal brain herniation to specific aspects of treatment have been fruitless,[1] suggesting to some that it is merely a marker of severity rather than the treatment administered. Several theories have been put forward as to why cerebral oedema develops as a complication of diabetic ketoacidosis[2] which include: haemoconcentration; stasis and local cerebral anoxia; abnormal capillary permeability allowing sodium ions to diffuse freely into cells; rapid reduction in blood glucose concentration following insulin therapy, resulting in disparity with cerebrospinal fluid glucose concentration, which then results in a marked osmotic shift of water across the blood brain barrier; accumulation of 'polyols', creating an osmotic gradient in the white matter; and, paradoxical lowering of cerebrospinal fluid pH in relation to blood pH related to bicarbonate administration, which may lead directly to local cerebral hypoxia. A concern in the clinical literature has been the possibility that some aspect of fluid administration or glucose therapy may contribute to the development of cerebral oedema. It should however be remembered that in severe cases of diabetic ketoacidosis cerebral oedema may well be a universal feature, which may even be present before treatment is initiated.[3–6] In a review of 17 case reports Rosenbloom *et al*.[7] identified no specific factor as being associated with the development of the cerebral oedema. This review did not substantiate that overrapid rehydration or correction of blood glucose was a feature common to all cases. In contrast, Duck and Wyatt[3] have argued that rapid fluid therapy (>4 l m^{-2} day^{-1}), together with the development of hyponatraemia or fall in calculated sodium at the time of falling glucose is a significant factor in the production of cerebral oedema. More recently in 1990, in a retrospective review of 119 patients, Harris *et al*.[8,9] observed that complications attributable to cerebral oedema were more likely to occur among patients with failure of their concentration of sodium to rise as glucose declined. In view of this, these authors then studied prospectively 58 episodes of diabetic ketoacidosis in 40 patients aged between 18 months and 20 years. By using a 48 h treatment plan to provide fluid replacement for dehydration (with half the deficit in sodium being given in the first 12 h of treatment), they found that the serum sodium concentration rose as glucose declined in 55 (95 %) of the 58 episodes. Importantly no patient developed a major complication. Their two main conclusions were: (1) failure of the serum sodium concentration to rise as glucose concentration declined is a marker of excessive administration of free water; (2) an expanded rehydration period, with repair fluid containing an average of 125 mmol l^{-1} of sodium early in therapy, will usually protect against a rapid decline in effective serum osmolality.

While there is no absolute standard for fluid resuscitation and treatment in children with diabetic ketoacidosis, there are certain principles that the majority of physicians would accept.[10] These include an initial rapid correction of hypovolaemia with isotonic fluid such as normal saline (containing 150 mmol l^{-1} of sodium), which is then followed by a phase of replacing the estimated fluid deficit over the next 24 to 28 h. Generally half of the calculated deficit is replaced over the first 8 to 12 h of treatment. In addition urinary losses and insensible requirement (approximately 40 % of usual maintenance) are given. After the first 8 h of therapy hyperglycaemia should be mild or resolved, and ongoing urinary losses need not be replaced. After the initial resuscitation phase, the type of fluid used for intravenous therapy is tailored to the patient's serum electrolytes. Insulin is usually started within 1–2 h of treatment. Finally, as stated by Krane,[10] 'prudence would indicate that if hypotonic fluids are used for rehydration of the child with diabetic ketoacidosis, serum sodium should be followed closely, and the amount of sodium in the intravenous fluid increased if the serum sodium declines'.

V.V. Khadilkar[1], F.J. Cameron[1], K.C. Hawkins[2], R.C. Tasker[2]
Departments of [1]Endocrinology and [2]Intensive Care, Great Ormond Street Hospital for Children, London, UK

References

1 Winegrad AI, Kern EFO, Simmons DA. Cerebral edema in diabetic ketoacidosis [Editorial]. *N Engl J Med* 1985; **312**: 1184–1185.
2 Greene SA, Jefferson IG, Baum JD. Cerebral oedema complicating diabetic ketoacidosis. *Dev Med Child Neurology* 1990; **32**: 633–644.
3 Duck RS, Wyatt DT. Factors associated with brain herniation in the treatment of diabetic ketoacidosis. *J Pediatr* 1988; **113**: 10–14.
4 Clements RS, Blumenthal SA, Morrison AD, Winegrad AI. Increased cerebrospinal fluid pressure during treatment of diabetic ketosis. *Lancet* 1971; **2**: 671–675.
5 Flein IA, Rackow EC, Sprung CL, Grodman R. Relation of colloid osmotic pressure to arterial hypoxemia and cerebral edema. *Ann Intern Med* 1982; **96**: 570–575.
6 Krane EJ, Rockoff MA, Wallman JK, Wolfsdorf JI. Subclinical brain swell-

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